Remarks

Claims 1-22 are canceled. Claims 23 and 26 are amended herein. Claims 24, 25, 27-36 are withdrawn from consideration. New claims 37-39 are added herein

Support for the amendment of claim 23 can be found throughout the original specification, for example on page 1, lines 1-7 and page 2. Claim 26 is amended to correct form. Support for new claims 37-39 can be found throughout the original specification, for example on page 3, lines 20-23 and pages 21-22.

Applicants believe no new matter is added by this amendment. Reconsideration of the subject application is respectfully requested.

Specification

Arrangement of the Specification

In response to the Examiner's suggestion relating to the arrangement of the specification, the Applicants have deleted "Appendix A" and has incorporated the entire contents thereof into the examples following the heading "Recombinant AcrV Vaccine Trial" on page 15. The Applicants have made every effort to use headings acceptable to the U.S. Patent and Trademark Office. The Applicants have also taken the opportunity to amend the title of the invention by deleting the word "novel", and to correct a typographical error in the paragraph appearing at lines 1 to 7 of page 5.

Inclusion of Embedded Hyperlinks

In response to the Examiner's objection relating to the inclusion of embedded hyperlinks on page 8, the Applicants have amended the paragraph appearing at lines 24 to 34 of page 8 by deleting the hyperlink text. The deleted hyperlink text was included in the original specification to facilitate easy access by a reader to the specific software utilized by the Applicants for sequence data analysis, but suitable information about the software may also be found in the references noted in the amended paragraph.

Sequence Listing and Sequence Identifiers

In response to the Examiner's objection relating to the absence from Table 2 of suitable sequence identifiers, the Applicants provide herewith a revised Table 2 in which the heading "Position" has been replaced with the heading "Residue Nos. of SEQ ID NO:10" to clarify that the oligonucleotide primers of Table 2 are derived from the isolated 5.7 kb

nucleic acid fragment (SEQ ID NO: 10) containing the type III secretion genes of *Aeromonas salmonicida*. A revised Sequence Listing is also submitted herewith to include synthetic oligonucleotide primers AsascrVt-L, AsacrVt-R, AsacrVN'-R, AsacrVC'-L, and AsacrVC'-R, each of which are based on specified residues of SEQ ID NO: 10 (see Table 2), but also include additional nucleotides added to the 5' end to create restriction enzyme recognition sites for cloning. Table 2 has also been amended to refer to appropriate sequence identifiers for the primers that include additional nucleotides at the 5'end, namely AsascrVt-L, AsacrVt-R, AsacrVN'-R, AsacrVC'-L, and AsacrVC'-R (SEQ ID NOs: 11-15).

Spelling

In response to the Examiner's concerns relating to the spelling of the word "characterised" and the use of the abbreviation "mio", the Applicants have amended the paragraphs appearing at lines 11 to 16 of page 1 and 16 to 24 of page 12.

The Applicants would be pleased to provide a replacement specification reflecting all of the amendments discussed herein if requested to do so by the Examiner.

Rejection Under 35 U.S.C. § 112, Second Paragarph

Claims 23 and 26 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly the designations AcrR is indefinite, in referring to either an E. coli polypeptide or an *A. salmonicida* polypeptide. Claims 23 is amended herein to specifically recite that the isolated polypeptide is present in *Aeromonas salmonicida*. Claim 26 depends from clam 23. The amendment of claim 23 precludes any possible confusion with local repressor AcrR of *E. coli*. Thus, Applicants submit that the amendment of claim 23 renders the rejection moot.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claim 26 was also rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled by the specification. The Examiner states that, although the specification is enabling for a vaccine composition comprising AcrV, enablement is not provided for all of the other listed peptides. The Applicants agree that the specification is enabling for a vaccine comprising AcrV, but respectfully disagree that it would require undue experimentation to produce vaccines including Acr1, Acr2, Acr3, Acr4, AcrD, AcrR, AcrG and/or AcrH.

The Examiner has performed a Wands analysis (*In re Wands*, 858 F.2d 731; 8 USPQ 2d 1400 (Fed. Cir. 1988). It is respectfully submitted that a complete review of the Wands factors does not support a rejection of claim 26 for a lack of enablement.

The Nature of the Invention

The claimed invention relates to immunogenic compositions (i.e. vaccines) comprising epitopic regions of the AcrI, Acr2, Acr3, Acr4, AcrD, AcrR, AcrG, AcrV and/or AcrH polypeptides, whose sequences are provided as Seq. ID Nos. 1 through 9 of the application. The compact Oxford dictionary (available on-line at askOxford.com) defines a vaccine as "a substance used to stimulate the production of antibodies and provide immunity against one or several diseases, prepared from the causative agent of a disease or a synthetic substitute."

The Breadth of the Claims

The claims are directed to immunogenic compositions comprising epitopic regions of an isolated AcrI, Acr2, Acr3, Acr4, AcrD, AcrR, AcrG, AcrV and/or AcrH polypeptide.

The State of the Prior Art

Aeromonas salmonicida is the etiological agent of furunculosis in salmonid fish. The disease is responsible for severe economic losses in intensively cultured salmon and trout. Protection of brook trout and Atlantic salmon has been achieved with a live attenuated vaccine (see for example, Vaughn et al., *Infect. Immun.* 61(3): 2172-2173, 1993). However, live vaccines are known to have side effects (see, for example, Elllis, *Dev Biol Stand.* 90:107-16, 1997).

The Predictability of the Art

Once a protein has been cloned and sequenced, a subunit vaccine can be produced. By way of example, vaccination of fish with CMV plasmids expressing protective antigens from Infectious Haematopoietic Necrosis Virus (IHNV) and Viral Haemorrhagic

Septicaemia Virus (VHSV) resulted in high-level protection against viral challenge (Anderson et al., "Genetic immunization of rainbow trout (Oncorhynchus mykiss) against infectious hematopoietic necrosis virus," Molec. *Marine Biol. Biotech.* 5, 105-113, 1996; Lorenzen; et al., "Protective immunity to VHS in rainbow trout (Oncorhynchus mykiss, Walbaum) following DNA vaccination," *Fish Shellfish Immunol.*, 1998).

Similarly, International Patent Application WO 2001/49712 and WO 2001/66569 provide examples of vaccinating fish with a subunit vaccine for ISAV (Infectious Salmon Anaemia Virus); U.S. Patent Application US 2003/0165526 published September 4, 2003 provides examples of using a 17 kDa protein from Piscirickettsia salmonis in a subunit vaccine; International Patent Application 2005/035558 provides examples of using a recombinantly expressed protein vaccine containing VP2 and VP3 from Infectious Pancreatic Necrosis Virus (IPNV) and also proteins from P. salmonis; and International Patent Application WO 2005/014629 contains examples of using a p55 subunit vaccine to protect fish against Photobacterium damselae infection.

Noonan et al., in Recombinant Infectious Hematopoietic Necrosis Virus and Viral Hemorrhagic Septicemia Virus Glycoprotein Epitopes Expressed in Aeromonas salmonicida Induce Protective Immunity in Rainbow Trout (Oncorhynchus mykiss), Applied and Environmental Microbiology, 61:10, pp. 3286-3591 (Oct. 1995) demonstrate that recombinant proteins expressed in A. salmonicida protect fish against IHNV and VHSV (thus the recombinant proteins are a subunit vaccine). Copies of the cited references are submitted herewith as Exhibit A, for the Examiner's consideration.

The Presence of Working Examples

As noted in the Office Action, a working example of a subunit vaccine with AcrV is provided.

The Relative Skill of those in the Art

As noted by the Examiner, the relative skill of an ordinary molecular biologist is high.

The Quantity of Experimentation Required

Exemplary protein sequences are provided for isolated Acr1, Acr2, Acr3, Acr4, AcrD, AcrR, AcrG, AcrV and/or AcrH polypeptides. In addition, an exemplary composition including AcrV that can be used to vaccinate fish is provided. One of skill in the art could readily use routine molecular biology techniques to synthesize the Acr1, Acr2, Acr3, Acr4, AcrD, AcrR, AcrG and/or AcrH proteins and substitute one or more of these proteins for AcrV protein in the vaccine formulation.

In view of the above Wands analysis, the Applicants submit that claim 26 is fully enabled by the specification. Reconsideration and withdrawal of the rejection is respectfully requested.

New claims

New claims 37 and 38 are directed to isolated polypeptides and immunogenic compositions comprising the amino acid sequence of one of SEQ ID NOs: 1 through 9 of the application, and corresponds generally to amended claims 23 and 26, in which the polypeptides are identified by the name (Acr1, Acr2, Acr3, Acr4, AcrD, AcrR, AcrG, AcrV and AcrH) ascribed to them by the Applicants. New claim 39 is directed to that part of claim 26 that the Examiner has indicated was not rejected under 35 U.S.C. § 112.

Conclusion

Applicants believe that the pending claims are now in condition for allowance, which action is requested. If any minor matters remain to be addressed before a Notice of Allowance is issued, the Examiner is respectfully requested to contact the undersigned for a telephone interview.

Respectfully submitted,

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